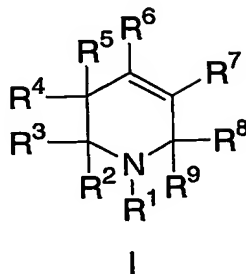


WHAT IS CLAIMED IS:

1. A compound according to Formula I:



5 wherein;

a is 0 or 1;

b is 0 or 1;

m is 0, 1, or 2;

10 n is 0 or 1;

r is 0 or 1;

s is 0 or 1;

R¹ is selected from:

- | | |
|----|---|
| 15 | 1) (C ₁ -C ₆ -alkylene) _n (C=X)C ₁ -C ₁₀ alkyl; |
| | 2) (C ₁ -C ₆ -alkylene) _n (C=X)aryl; |
| | 3) (C ₁ -C ₆ -alkylene) _n (C=X)C ₂ -C ₁₀ alkenyl; |
| | 4) (C ₁ -C ₆ -alkylene) _n (C=X)C ₂ -C ₁₀ alkynyl; |
| | 5) (C ₁ -C ₆ -alkylene) _n (C=X)C ₃ -C ₈ cycloalkyl; |
| 20 | 6) (C ₁ -C ₆ -alkylene) _n (C=X)heterocyclyl; |
| | 7) (C ₁ -C ₆ -alkylene) _n (C=X)NR ^c R ^{c'} ; |
| | 8) (C ₁ -C ₆ -alkylene) _n SO ₂ NR ^c R ^{c'} ; |
| | 9) (C ₁ -C ₆ -alkylene) _n SO ₂ C ₁ -C ₁₀ alkyl; |
| | 10) (C ₁ -C ₆ -alkylene) _n SO ₂ C ₂ -C ₁₀ alkenyl; |
| 25 | 11) (C ₁ -C ₆ -alkylene) _n SO ₂ C ₂ -C ₁₀ alkynyl; |
| | 12) (C ₁ -C ₆ -alkylene) _n SO ₂ -aryl; |
| | 13) (C ₁ -C ₆ -alkylene) _n SO ₂ -heterocyclyl; |
| | 14) (C ₁ -C ₆ -alkylene) _n SO ₂ -C ₃ -C ₈ cycloalkyl; |

15) $(C_1-C_6\text{-alkylene})_n P(=O)R^d R^{d'}$;

16) aryl;

17) heterocyclyl; and

18) C_1-C_{10} alkyl;

5 said alkyl, aryl, alkenyl, alkynyl, cycloalkyl, alkylene, heteroaryl and heterocyclyl is optionally substituted with one or more substituents selected from R^{10} ;

R^2 , R^3 , R^4 , R^5 and R^9 are independently selected from:

1) H;

2) $(C=O)_r O_s (C_1-C_{10})$ alkyl;

3) $O_r (C_1-C_3)$ perfluoroalkyl;

4) (C_0-C_6) alkylene- $S(O)_m R^a$;

5) oxo;

6) OH;

7) halo;

8) CN;

9) $(C=O)_r O_s (C_2-C_{10})$ alkenyl;

10) $(C=O)_r O_s (C_2-C_{10})$ alkynyl;

11) $(C=O)_r O_s (C_3-C_6)$ cycloalkyl;

12) $(C=O)_r O_s (C_0-C_6)$ alkylene-aryl;

13) $(C=O)_r O_s (C_0-C_6)$ alkylene-heterocyclyl;

14) $(C=O)_r O_s (C_0-C_6)$ alkylene- $N(R^b)_2$;

15) $C(O)R^a$;

16) (C_0-C_6) alkylene- $CO_2 R^a$;

17) $C(O)H$;

18) (C_0-C_6) alkylene- $CO_2 H$;

19) $C(O)N(R^b)_2$;

20) $S(O)_m R^a$; and

21) $S(O)_2 N(R^b)_2$;

30 said alkyl, alkenyl, alkynyl, cycloalkyl, aryl, alkylene and heterocyclyl is optionally substituted with up to three substituents selected from R^b , OH, (C_1-C_6) alkoxy, halogen, $CO_2 H$, CN, $O(C=O)C_1-C_6$ alkyl, oxo, and $N(R^b)_2$;

R^6 and R^8 are selected from:

1) alkyl;

- 2) C₃-C₈ cycloalkyl;
- 3) aryl; and
- 4) heterocyclyl;

said alkyl, cycloalkyl, aryl and heterocyclyl are optionally substituted with up to 3 substituents
 5 selected from R¹³;

R⁷ is:

- 1) H;
- 2) C₁-C₁₀ alkyl;
- 3) C₂-C₁₀ alkenyl;
- 4) C₂-C₁₀ alkynyl;
- 5) CN;
- 6) halo;
- 7) CO₂H;
- 8) (C₁-C₆)alkyl amino; and
- 9) (C₁-C₆)alkyl hydroxy;

R¹⁰ is:

- 1) (C=O)_aO_bC₁-C₁₀ alkyl;
- 2) (C=O)_aO_baryl;
- 3) C₂-C₁₀ alkenyl;
- 4) C₂-C₁₀ alkynyl;
- 5) (C=O)_aO_b heterocyclyl;
- 6) CO₂H;
- 7) halo;
- 8) CN;
- 9) OH;
- 10) O_bC₁-C₆ perfluoroalkyl;
- 11) O_a(C=O)_bNR¹¹R¹²;
- 12) S(O)_mR^a;
- 13) S(O)₂NR¹¹R¹²;
- 14) oxo;
- 15) CHO;
- 16) (N=O)R¹¹R¹²; or
- 17) (C=O)_aO_bC₃-C₈ cycloalkyl;

said alkyl, aryl, alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted with one or more substituents selected from R¹³;

R¹¹ and R¹² are independently selected from:

- 5 1) H;
- 2) (C=O)O_bC₁-C₁₀ alkyl;
- 3) (C=O)O_bC₃-C₈ cycloalkyl;
- 4) (C=O)O_baryl;
- 5) (C=O)O_bheterocyclyl;
- 10 6) C₁-C₁₀ alkyl;
- 7) aryl;
- 8) C₂-C₁₀ alkenyl;
- 9) C₂-C₁₀ alkynyl;
- 10) heterocyclyl;
- 15 11) C₃-C₈ cycloalkyl;
- 12) SO₂R^a;
- 13) (C=O)NR^b₂;
- 14) oxo; and
- 15) OH;

20 said alkyl, cycloalkyl, aryl, heterocyclyl, alkenyl, and alkynyl is optionally substituted with one or more substituents selected from R¹³; or

R¹¹ and R¹² can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 4-7 members in each ring and optionally containing, in
 25 addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one or more substituents selected from R¹³;

R¹³ is selected from:

- 30 1) (C=O)_rO_s(C₁-C₁₀)alkyl;
- 2) O_r(C₁-C₃)perfluoroalkyl;
- 3) (C₀-C₆)alkylene-S(O)_mR^a;
- 4) oxo;
- 5) OH;
- 35 6) halo;

- 7) CN;
 8) $(C=O)_rO_s(C_2-C_{10})$ alkenyl;
 9) $(C=O)_rO_s(C_2-C_{10})$ alkynyl;
 10) $(C=O)_rO_s(C_3-C_6)$ cycloalkyl;
 5 11) $(C=O)_rO_s(C_0-C_6)$ alkylene-aryl;
 12) $(C=O)_rO_s(C_0-C_6)$ alkylene-heterocyclyl;
 13) $(C=O)_rO_s(C_0-C_6)$ alkylene-N(R^b)₂;
 14) C(O)R^a;
 15) (C_0-C_6) alkylene-CO₂R^a;
 10 16) C(O)H;
 17) (C_0-C_6) alkylene-CO₂H;
 18) C(O)N(R^b)₂;
 19) S(O)_mR^a; and
 20) S(O)₂N(R^b)₂;

15 said alkyl, alkenyl, alkynyl, cycloalkyl, aryl, alkylene and heterocyclyl is optionally substituted with up to three substituents selected from R^b, OH, (C₁-C₆)alkoxy, halogen, CO₂H, CN, O(C=O)C₁-C₆ alkyl, oxo, and N(R^b)₂;

R^a is (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, aryl, or heterocyclyl;

20 said alkyl, cycloalkyl, aryl or heterocyclyl is optionally substituted with one or more substituents selected from R^f;

R^b is H, (C₁-C₆)alkyl, aryl, heterocyclyl, (C₃-C₆)cycloalkyl, (C=O)OC₁-C₆ alkyl, (C=O)C₁-C₆ alkyl or S(O)₂R^a;

25 said alkyl, cycloalkyl, aryl or heterocyclyl is optionally substituted with one or more substituents selected from R^f;

30 R^c and R^{c'} are independently selected from: H, (C₁-C₆)alkyl, aryl, heterocyclyl and (C₃-C₆)cycloalkyl, optionally substituted with one, two or three substituents selected from R¹³, or

R^c and R^{c'} can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 4-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said

monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from R¹³;

R^d and R^{d'} are independently selected from: (C₁-C₆)alkyl, (C₁-C₆)alkoxy and NR^b₂, or

R^d and R^{d'} can be taken together with the phosphorous to which they are attached to form a monocyclic heterocycle with 4-7 members the ring and optionally containing, in addition to the phosphorous, one or two additional heteroatoms selected from NR^e, O and S, said monocyclic heterocycle optionally substituted with one, two or three substituents selected from R¹³;

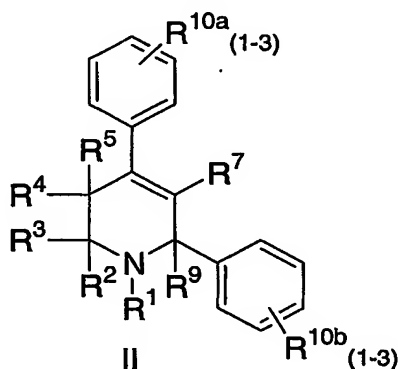
R^e is selected from: H and (C₁-C₆)alkyl;

R^f is selected from: heterocyclyl, amino substituted heterocyclyl, (C₁-C₆)alkyl, amino (C₁-C₆)alkyl, (C₁-C₆)alkyl amino, hydroxy (C₁-C₆)alkyl, OH and NH₂; and

X is selected from O, NR^e and S;

or a pharmaceutically acceptable salt or stereoisomer thereof.

2. The compound according to Claim 1, as illustrated by Formula II:



wherein:

R^{10a} and R^{10b} are independently selected from:

- 1) H;
- 2) C₁-C₁₀ alkyl;
- 3) C₂-C₁₀ alkenyl;

- 4) C₂-C₁₀ alkynyl;
- 5) OH;
- 6) CN;
- 7) halo;
- 8) CHO;
- 9) CO₂H;
- 10) (C₁-C₆)alkyl amino; and
- 11) (C₁-C₆)alkyl hydroxy;

and all other substituents and variables are as defined in Claim 1;

or a pharmaceutically acceptable salt or stereoisomer thereof.

3. The compound according to Claim 2 wherein:

R¹ is selected from:

- 1) (C₁-C₆-alkylene)_n(C=X)C₁-C₁₀ alkyl;
- 2) (C₁-C₆-alkylene)_n(C=X)aryl;
- 3) (C₁-C₆-alkylene)_n(C=X)C₂-C₁₀ alkenyl;
- 4) (C₁-C₆-alkylene)_n(C=X)C₂-C₁₀ alkynyl;
- 5) (C₁-C₆-alkylene)_n(C=X)C₃-C₈ cycloalkyl;
- 6) (C₁-C₆-alkylene)_n(C=X)heterocyclyl;
- 7) (C₁-C₆-alkylene)_n(C=X)NR^cR^{c'};
- 8) (C₁-C₆-alkylene)_nSO₂NR^cR^{c'};
- 9) (C₁-C₆-alkylene)_nSO₂C₁-C₁₀ alkyl;
- 10) (C₁-C₆-alkylene)_nSO₂-aryl;
- 11) (C₁-C₆-alkylene)_nSO₂-heterocyclyl;
- 12) (C₁-C₆-alkylene)_nSO₂-C₃-C₈ cycloalkyl;
- 13) (C₁-C₆-alkylene)_nP(=O)R^dR^{d'};
- 14) aryl;
- 15) heterocyclyl; and
- 16) C₁-C₁₀ alkyl;

said alkyl, aryl, alkenyl, alkynyl, cycloalkyl, alkylene, heteroaryl and heterocyclyl is optionally substituted with one or more substituents selected from R¹⁰;

and all other substituents and variables are as defined in Claim 2;

or a pharmaceutically acceptable salt or stereoisomer thereof.

5 4. The compound according to Claim 3 wherein:

R¹ is selected from:

- 1) (C=O)C₁-C₁₀ alkyl;
- 2) (C=O)aryl;
- 10 3) (C=O)C₂-C₁₀ alkenyl;
- 4) (C=O)C₂-C₁₀ alkynyl;
- 5) (C=O)C₃-C₈ cycloalkyl;
- 6) (C=O)NR^cR^{c'};
- 7) SO₂NR^cR^{c'};
- 15 8) SO₂C₁-C₁₀ alkyl;
- 9) SO₂-aryl;
- 10) SO₂-heterocyclyl;
- 11) SO₂-C₃-C₈ cycloalkyl; and
- 12) P(=O)R^dR^{d'};

20 said alkyl, aryl, alkenyl, alkynyl, cycloalkyl, alkylene, heteroaryl and heterocyclyl is optionally substituted with one or more substituents selected from R¹⁰;

R², R³, R⁴, R⁵ and R⁹ are independently:

- 1) H;
- 25 2) C₁-C₁₀ alkyl;
- 3) C₂-C₁₀ alkenyl;
- 4) C₂-C₁₀ alkynyl;
- 5) CHO;
- 6) CO₂H;
- 30 7) (C₁-C₆)alkyl amino;
- 8) (C₁-C₆)alkyl hydroxy;
- 9) (C=O)_rO_s(C₁-C₁₀)alkyl; and
- 10) C(O)N(R^b)₂

35 R⁷ is:

- 1) H;
- 2) (C₁-C₆)alkyl amino; and
- 3) (C₁-C₆)alkyl hydroxy;

5 and all other substituents and variables are as defined in Claim 3;

or a pharmaceutically acceptable salt or stereoisomer thereof.

5. The compound according to Claim 4 wherein:

10

R¹ is selected from:

- 1) (C=O)NR^cR^{c'};
- 2) SO₂NR^cR^{c'};
- 3) SO₂C₁-C₁₀ alkyl; and
- 15 4) (C=O)C₁-C₁₀ alkyl;

said alkyl is optionally substituted with one, two or three substituents selected from R¹⁰;

and all other substituents and variables are as defined in Claim 4;

20 or a pharmaceutically acceptable salt or stereoisomer thereof.

6. A compound selected from:

3-[1-Acetyl-4-(2,5-difluorophenyl)-1,2,5,6-tetrahydropyridin-2-yl]phenol;

25

1-acetyl-4-(2,5-difluorophenyl)-6-phenyl-1,2,3,6-tetrahydropyridine;

4-(2,5-difluorophenyl)-6-phenyl-3,6-dihydropyridine-1(2H)-carboxamide;

30 N11-[4-(2,5-difluorophenyl)-6-(3-hydroxyphenyl)-1-L-valyl-1,2,3,6-tetrahydropyridin-2-yl]-L-valinamide; and

4-(2,5-difluorophenyl)-6-(3-hydroxyphenyl)-N-methyl-N-[2-methyl-3-(methylamino)propyl]-3,6-dihydropyridine-1(2H)-carboxamide;

35

or a pharmaceutically acceptable salt or stereoisomer thereof.

7. A TFA salt selected from:

5 N-1-[4-(2,5-difluorophenyl)-6-(3-hydroxyphenyl)-1-L-valyl-1,2,3,6-tetrahydropyridin-2-yl]-L-valinamide; and

4-(2,5-difluorophenyl)-6-(3-hydroxyphenyl)-N-methyl-N-[2-methyl-3-(methylamino)propyl]-3,6-dihydropyridine-1(2H)-carboxamide;

10

or a stereoisomer thereof.

8. The compound according to Claim 6 which is selected from:

15 3-[1-Acetyl-4-(2,5-difluorophenyl)-1,2,5,6-tetrahydropyridin-2-yl]phenol; and

N-1-[4-(2,5-difluorophenyl)-6-(3-hydroxyphenyl)-1-L-valyl-1,2,3,6-tetrahydropyridin-2-yl]-L-valinamide;

20 or a pharmaceutically acceptable salt or stereoisomer thereof.

9. A compound according to Claim 1 which is selected from:

25 6-(2-aminoethyl)-4-(2,5-difluorophenyl)-N,N-dimethyl-6-phenyl-3,6-dihydropyridine-1(2H)-carboxamide;

6-(3-aminopropyl)-4-(2,5-difluorophenyl)-N,N-dimethyl-6-phenyl-3,6-dihydropyridine-1(2H)-carboxamide;

30 6-(4-aminobutyl)-4-(2,5-difluorophenyl)-N,N-dimethyl-6-phenyl-3,6-dihydropyridine-1(2H)-carboxamide;

4-(2,5-difluorophenyl)-6-(hydroxymethyl)-6-(3-hydroxyphenyl)-N-methyl-N-(1-methylpiperidin-4-yl)-3,6-dihydropyridine-1(2H)-carboxamide;

35

3-[1-[(2S)-2-amino-2-cyclopropylethanoyl]-4-(2,5-difluorophenyl)-2-(hydroxymethyl)-1,2,5,6-tetrahydropyridin-2-yl]phenol;

4-(2,5-difluorophenyl)-6-(hydroxymethyl)-6-(3-hydroxyphenyl)-N,N-dimethyl-3,6-dihydropyridine-1(2H)-carboxamide;

6-(3-aminopropyl)-4-isopropyl-N,N-dimethyl-6-phenyl-3,6-dihydropyridine-1(2H)-carboxamide;

6-(3-aminopropyl)-6-(3-hydroxyphenyl)-4-isopropyl-N,N-dimethyl-3,6-dihydropyridine-1(2H)-carboxamide;

2-[1-acetyl-4-(2,5-difluorophenyl)-2-phenyl-1,2,5,6-tetrahydropyridin-2-yl]ethanamine;

3-[1-acetyl-4-(2,5-difluorophenyl)-2-phenyl-1,2,5,6-tetrahydropyridin-2-yl]propan-1-amine;

4-[1-acetyl-4-(2,5-difluorophenyl)-2-phenyl-1,2,5,6-tetrahydropyridin-2-yl]butan-1-amine;

3-[1-acetyl-2-(2-aminoethyl)-4-(2,5-difluorophenyl)-1,2,5,6-tetrahydropyridin-2-yl]phenol;

3-[1-acetyl-2-(3-aminopropyl)-4-(2,5-difluorophenyl)-1,2,5,6-tetrahydropyridin-2-yl]phenol;

3-[1-acetyl-2-(4-aminobutyl)-4-(2,5-difluorophenyl)-1,2,5,6-tetrahydropyridin-2-yl]phenol;

3-[1-acetyl-2-(2-aminoethyl)-4-(2,5-difluorophenyl)-1,2,5,6-tetrahydropyridin-2-yl]phenol;

1'-acetyl-4'-(2,5-difluorophenyl)-1',2',5',6'-tetrahydro-2,2'-bipyridin-6(1H)-one; and

1-acetyl-4-(2,5-difluorophenyl)-1,2,5,6-tetrahydro-2,4'-bipyridin-2'(1'H)-one;

or a pharmaceutically acceptable salt or stereoisomer thereof.

10. A pharmaceutical composition comprising a pharmaceutical carrier, and dispersed therein, a therapeutically effective amount of a compound of Claim 1.

11. A method for treating cancer which comprises administering to a mammal in need thereof a therapeutically effective amount of a compound of Claim 1.

12. A pharmaceutical composition made by combining the compound of Claim 1 and a pharmaceutically acceptable carrier.

13. A process for making a pharmaceutical composition comprising combining a compound of Claim 1 and a pharmaceutically acceptable carrier.

14. The composition of Claim 10 further comprising a second compound selected from: an estrogen receptor modulator, an androgen receptor modulator, a retinoid receptor modulator, a cytotoxic/cytostatic agent, an antiproliferative agent, a prenyl-protein transferase inhibitor, an HMG-CoA reductase inhibitor, an HIV protease inhibitor, a reverse transcriptase inhibitor, an angiogenesis inhibitor, a PPAR- γ agonist, a PPAR- δ agonist; an inhibitor of cell proliferation and survival signaling, an agent that interferes with a cell cycle checkpoint, and an apoptosis inducing agent.

15. The composition of Claim 14, wherein the second compound is an angiogenesis inhibitor selected from the group consisting of a tyrosine kinase inhibitor, an inhibitor of epidermal-derived growth factor, an inhibitor of fibroblast-derived growth factor, an inhibitor of platelet derived growth factor, an MMP (matrix metalloprotease) inhibitor, an integrin blocker, interferon- α , interleukin-12, pentosan polysulfate, a cyclooxygenase inhibitor, carboxyamidotriazole, combretastatin A-4, squalamine, 6-O-chloroacetyl-carbonyl)-fumagillol, thalidomide, angiostatin, troponin-1, or an antibody to VEGF.

16. The composition of Claim 14, wherein the second compound is an estrogen receptor modulator selected from tamoxifen and raloxifene.

17. A method of treating cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with radiation therapy.

18. A method of treating or preventing cancer which comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with a compound selected from: an estrogen receptor modulator, an androgen receptor modulator, retinoid receptor

modulator, a cytotoxic/cytostatic agent, an antiproliferative agent, a prenyl-protein transferase inhibitor, an HMG-CoA reductase inhibitor, an HIV protease inhibitor, a reverse transcriptase inhibitor, an angiogenesis inhibitor, a PPAR- γ agonists, a PPAR- δ agonist, an inhibitor of inherent multidrug resistance, an anti-emetic agent, an agent useful in the treatment of anemia,
5 an agent useful in the treatment of neutropenia, an immunologic-enhancing drug, an inhibitor of cell proliferation and survival signaling, an agent that interferes with a cell cycle checkpoint, and an apoptosis inducing agent.

19. A method of treating cancer which comprises administering a
10 therapeutically effective amount of a compound of Claim 1 in combination with radiation therapy and a compound selected from: an estrogen receptor modulator, an androgen receptor modulator, retinoid receptor modulator, a cytotoxic/cytostatic agent, an antiproliferative agent, a prenyl-protein transferase inhibitor, an HMG-CoA reductase inhibitor, an HIV protease inhibitor, a reverse transcriptase inhibitor, an angiogenesis inhibitor, a PPAR- γ agonists, a
15 PPAR- δ agonist, an inhibitor of inherent multidrug resistance, an anti-emetic agent, an agent useful in the treatment of anemia, an agent useful in the treatment of neutropenia, an immunologic-enhancing drug, an inhibitor of cell proliferation and survival signaling, an agent that interferes with a cell cycle checkpoint, and an apoptosis inducing agent.

20. A method of treating or preventing cancer which comprises administering
20 a therapeutically effective amount of a compound of Claim 1 and paclitaxel or trastuzumab.

21. A method of treating or preventing cancer which comprises administering
25 a therapeutically effective amount of a compound of Claim 1 and a COX-2 inhibitor.